REMARKS

In the specification, paragraphs 0003, 0041 and 0052 have been amended. Claim 5 also is amended. Claims 1-14 are pending in this application.

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

## I. RESTRICTION REQUIREMENT

Applicants hereby renew their request for reconsideration of the imposed restriction requirement. Applicants devised a new way to determine the presence or absence of a micro-organism harboring a beta-lactamase exhibiting resistance to particular beta-lactam antibiotics. To this end, the micro-array put to use in the present method contains on predetermined locations thereon a plurality of sets of nucleotide sequences of the general formula R1-(X)-R2. Contrary to the examiner's assertion, the formula R1-(X)-R2 does not "apply to any nucleotide sequence in any gene or genome." Rather, R1-(X)-R2 are derived from the beta-lactamase gene. Accordingly, request that the restriction requirement be withdrawn.

## II. REJECTIONS UNDER 35 U.S.C. § 112 ¶2

The examiner rejects claims 1-13 for alleged indefiniteness. In particular, the examiner asserts that it is unclear whether "R1 and R2 together comprise about 5 to 20 nucleotides or if R1 comprises about 5 to 20 nucleotides and R2 comprises about 5 to 20 nucleotides." Applicants respectfully traverse the rejection.

Claim 1 specifically states that "R1 and R2 **each** have a length of from about 3 to 20 nucleotides." (emphasis added) Thus, one of ordinary skill in the art would readily recognize that R1 comprises about 5 to 20 nucleotides, and R2 comprises about 5 to 20 nucleotides. Accordingly, the rejection should be withdrawn.

## III. REJECTIONS UNDER 35 U.S.C. § 103

The examiner rejects claims 1-6, 8, 9, 11 and 13 under 35 U.S.C. §103(a) for allegedly being unpatentable over Lee et al. in view of Blazquez et al., Chee et al. (A) (WO 95/11995) and Sutcliffe. Applicants respectfully traverse the rejection.

In levying an obviousness rejection under 35 U.S.C. 103, the examiner has the burden of establishing (1) some suggestion or motivation to modify the reference or to combine reference teachings, (2) a reasonable expectation of success, and (3) that the prior art references, when combined, teach or suggest all the claim limitations. *See* MPEP §2143 (May 2004). "Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438 (Fed. Cir. 1991). In the pending case, the examiner has failed to satisfy this burden.

The examiner cites Lee for disclosing a micro-array for the detection of various beta-lactamase resistant genes. In this regard, the examiner correctly notes that Lee fails to teach the capture probes of the claimed methods. Contrary to the examiner's assertions, however, the secondary references do not cure the defects of the primary reference.

Blazquez is cited for teaching that amino acid replacement at seven residues of the TEM1 gene can alter resistance of microorganisms to specific antibiotics. Meanwhile, Chee (A) is cited for teaching a tilling array, and Sutcliffe is cited for disclosing the nucleotide sequence of the beta-lactamase gene. The cited materials, however, do not disclose a set of capture probes comprising the sequence $R^1$-(X)-$R^2$, which sequence represents a selected part of the sequence of a beta-lactamase gene, wherein X represents a nucleotide triplet and its permutations, and wherein $R^1$ and $R^2$ each have a length of from about 3 to 20 nucleotides. Similarly, the cited materials fail to disclose or suggest using sets of such capture probes in a method for detecting the presence of a beta-lactam resistant micro-organism in a biological sample and simultaneously determining the genotype of the beta-lactam resistance such that an adjacent set starts at a given position 3n of nucleotides down-stream from the first set of capture probes, wherein n is an integer of 1 to 10, so that the nucleotide sequence of the beta-

lactamase gene is covered over a desired range. Thus, no combination of the cited references presages the claimed invention.

Furthermore, the examiner has failed to make the requisite showing of a motivation to combine the cited references. In particular, the examiner has failed to provide any "objective evidence of record" that an artisan at the time of the invention would have been motivated to combine, for example, the micro-array of Lee with the tilling array of Chee (A). *In re Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002).

Moreover, Lee teaches away from the claimed invention. Lee utilizes long probes to detect resistant genes. For example, the probe for the OXY antibiotic resistant gene is more than 700 nt. *See* Table 1, providing primers used to prepare the probe DNAs for chips. Such long probes are incompatible with the SNP detection investigated by the claimed methods, which requires very short probes.

The examiner also rejects claim 7 under 35 U.S.C. §103(a) for allegedly being unpatentable over Lee et al. in view of Blazquez et al., Chee et al. (A) (WO 95/11995) and Sutcliffe and in further view of Osano et al. Applicants respectfully traverse the rejection.

Claim 7, which depends from claim 5 and thereby ultimately from claim 1, adds the limitation that the beta-lactamase is a serine- or zinc- beta-lactamase. The limitations of Lee, Blazquez and Chee (A) are discussed above. The cited portions of Osano do not cure the defects of the primary reference or the other secondary references. Thus, no combination of the cited references presages the claimed invention.

The examiner also rejects claim 10 under 35 U.S.C. §103(a) for allegedly being unpatentable over Lee et al. in view of Blazquez et al., Chee et al. (A) (WO 95/11995) and Sutcliffe and in further view of Chee et al. (B) and Routier. The examiner further rejects claim 12 under 35 U.S.C. §103(a) for allegedly being unpatentable over Lee et al. in view of Blazquez et al., Chee et al. (A) (WO 95/11995) and Sutcliffe and in further view of Behrensdor. Applicants respectfully traverse the rejections.

Claim 10, which depends from claim 4 and ultimately from claim 1, adds the limitation that the target DNA is fragmented to fragments having a size of about 15 to about 50 bp. Claim 12, which depends from claim 1, adds the limitation that the DNA is labeled after the contacting step. The short-comings of Lee, Blazquez and Chee (A) are discussed above. The cited portions of neither Chee (B) nor Behrensdof cure the defects of the primary reference or the other secondary references. Thus, no combination of the cited references presages the claimed invention.

Accordingly, since the examiner has failed to establish a *prima facie* case of obviousness, the rejections should be withdrawn.

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Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date December 8, 2006

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